

Challenges to the Management of High-Risk Stroke Patients with Multiple-Site Occlusive Vascular Disease

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Key Words

Stroke · Peripheral arterial disease · Coronary artery disease · Evidence-based practice

Abstract

Stroke patients are at high risk of secondary vascular events. Although in the short term the risk of experiencing a second stroke is high, in the long term patients are more likely to have myocardial infarction. Many stroke patients have also developed polyvascular disease in the form of coronary artery disease and peripheral arterial disease, which is a marker of increased morbidity and mortality in patients with non-cardioembolic ischemic stroke. Despite the high risk of events in these patients, current evidence-based guidelines make very few recommendations that address the need to detect and manage polyvascular disease following a stroke. Optimised Stroke Care for Re-Admission Reduction in Europe (OSCARE) is an initiative that has been set up to address some of these shortcomings. Copyright © 2011 S. Karger AG, Basel

Introduction

Ischaemic stroke is associated with a significant burden to the patient, carers and health systems. Stroke is the second leading cause of death worldwide, with around 5.5 million deaths occurring in the 15 million people who have a stroke each year [1]. Approximately one third of stroke patients will be left permanently disabled, rendering stroke a leading cause of adult long-term disability. Hospital readmission due to a second cerebrovascular event is common with 20–27% of patients readmitted within the first year [2, 3]. However, over 10 years, the risk of recurrent stroke decreases and other vascular events are more common [2–4]. Patients who have experienced an atherothrombotic stroke often have atherothrombotic disease in other arterial territories (polyvascular disease, polyVD), most often in the form of coronary artery disease (CAD) and/or peripheral arterial disease (PAD) [5]. Recent results have highlighted the importance of polyVD as a marker of increased morbidity and mortality in these patients [6–8]. Despite these data, polyVD is often inadequately assessed and stroke patients with polyVD are frequently not diagnosed, investigated or treated optimally [9].

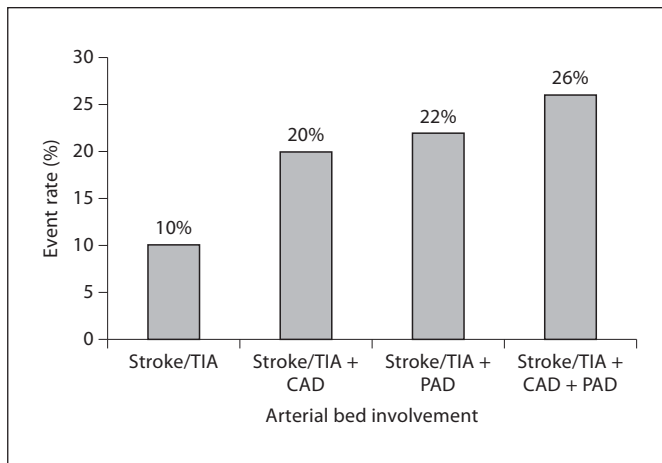


Fig. 1. One-year rates of CV death, MI, stroke or hospitalization in patients with cerebrovascular disease from the REACH registry [10].

The aim of this article is (1) to summarise the available data that stroke patients with polyVD have an increased morbidity and mortality, (2) to highlight unmet needs and areas where data are currently lacking, and (3) to introduce the Optimised Stroke Care for Re-Admission Reduction in Europe (OSCARE) initiative, designed to improve the care of high-risk stroke patients with polyVD

Stroke Patients with polyVD: A High-Risk Population

Table 1 summarises the evidence showing that polyVD is very common in patients with atherothrombotic stroke/transient ischaemic attack (TIA), and is associated with a high risk. The international Reduction of Atherothrombosis for Continued Health (REACH) registry of 67,888 patients with symptomatic atherothrombotic disease showed that 41% of patients with stroke/TIA (18,843 patients with predominantly non-cardiogenic ischaemic stroke) also had disease in at least one additional vascular territory [5, 10, 11]. Patients with documented polyVD have more than double the risk of a major event or hospitalisation at 1 year compared with patients in whom only the cerebral territory is involved (fig. 1) [12]. This was supported by a meta-analysis of 39 studies, involving 65,996 patients with stroke or TIA, where the 1-year rate of non-stroke vascular death was 2.1% and myocardial infarction (MI) was 2.2% [13]. The increased risk of recurrent stroke in patients with polyVD may in part be due to an increased variability in

blood pressure in these patients, probably due to increased vascular stiffness, which in itself is an independent risk factor for stroke [14, 15]. The Polyvascular Atherothrombosis Observational Study (PATHOS), Systematic Risk Evaluation in Ischaemic Stroke (SCALA) study and German Epidemiological Study of ABI (Get-ABI) showed that in patients with stroke/TIA, PAD (defined by the ankle-brachial index, $ABI \leq 0.9$) was also present in 33.5, 51 and 30.3% of cases, respectively [16]. PATHOS showed that the presence of PAD was associated with a 1.5-fold increased risk of adverse 1-year outcomes [17–19]; SCALA showed that the presence of PAD was associated with a 2-fold higher risk of recurrent stroke or cardiovascular death after 17.5 months [20]. It is important to note that asymptomatic PAD is much more common than symptomatic PAD [20], but is associated with a similar increase in risk [8, 21].

Seo et al. [16] showed that stroke/TIA increased the risk of CAD by 11-fold [2, 3], and Gongora-Rivera et al. [22] showed that CAD could be detected in >70% of patients who had died of stroke [22]. Furthermore, approximately 40% of these cases were clinically silent [8, 16–21].

polyVD is also associated with high economic cost burdens for healthcare systems. The presence of PAD or CAD in addition to stroke or TIA doubles the 1-year costs associated with hospitalisation for cardiovascular reasons (MI, stroke) as determined by the 1-year follow-up data of patients from the USA enrolled in the REACH registry [23].

What Is Missing from the Guidelines?

Despite the high frequency of stroke patients with atherothrombotic disease in additional vascular territories, and the increased risk that is associated with polyVD, current treatment guidelines do not specifically address the management of polyVD in patients who have experienced a stroke. Current guidelines do provide targets for many of the risk factors for atherothrombosis (blood pressure, lipids and blood glucose, among others). However, no routine screening for polyVD is recommended, and polyVD is, therefore, likely to frequently go undetected. In addition to its detection, no specific recommendations are made in the current guidelines for the long-term treatment and management of stroke patients with polyVD. One of the main reasons for this gap in the guidelines is the lack of evidence available in patients with stroke associated with polyVD [24].

Table 1. Summary of polyVD studies

Study	Design	Patients	Key findings
REACH (Bhatt et al., 2006; Steg et al., 2007) [5, 6, 10]	Registry	67,888 patients with symptomatic atherothrombotic disease, including 18,843 patients with stroke or TIA (predominantly non-cardiogenic atherothrombotic disease)	polyVD is very common and carries an increased risk 30% of stroke/TIA patients also had CAD; 5% also had PAD; 6% also had both CAD and PAD Polyvascular stroke/TIA more than doubles the risk of a major event or hospitalization at 1 year compared with monovascular stroke/TIA 22% of patients with stroke/TIA + PAD experienced MI, cardiovascular death and stroke, or hospitalization within 1 year 20% of patients with stroke/TIA + CAD experienced a major cardiovascular event within 1 year In patients with carotid artery stenosis ¹ , cardiovascular death, myocardial infarction or stroke was seen in 6.03% after 1 year (vs. 4.29% for patients without carotid artery stenosis)
Touze et al., 2005 [13]	Meta-analysis	65,996 patients with stroke or TIA, pooled from 39 studies	Atherothrombotic stroke is associated with events in other vascular territories 1-year rate of non-stroke vascular death was 2.1% (95% CI 1.9–2.4) and MI was 2.2% (95% CI 1.7–2.7) In studies specifically examining patients with TIA or stroke attributable to atherosclerosis, the risk of MI (4 studies) was 1.9% per year (95% CI, not estimable) and that of nonstroke vascular death (5 studies) was 2.3% per year (95% CI 1.9–2.7)
Touze et al., 2006 [34]	Prospective review of angiograms	2,741 patients with a recently symptomatic carotid stenosis (unilateral vs bilateral)	Bilateral carotid stenosis ² (due to atherosclerosis) is suggestive of generalized atherosclerotic disease, and is associated with increased event rates in other vascular territories Non-stroke-related vascular death has been shown to be associated with bilateral carotid artery disease (hazard ratio 2.0; 95% CI 1.5–2.6), again reflecting systemic disease
Seo et al., 2008 [16]	Observational study	71 patients with ischaemic stroke. CAD identified using CT coronary angiography	CAD is very common in patients with atherothrombotic stroke/TIA 25.4% of patients had significant CAD, and this was associated with the presence of atherosclerosis of the carotid artery. This represents an 11-fold increased risk of CAD compared with an age-matched control population
Gongora-Rivera et al., 2007 [22]	Autopsy study	803 consecutive autopsies of neurologic patients; 341 had stroke; 251 had brain infarction; and 60 had confirmed atherothrombotic stroke	Comorbid CAD is common and often asymptomatic Coronary artery plaques were found in 78.3% of cases with atherothrombotic stroke MI was evident in 36.7% of cases with atherothrombotic stroke In the overall cohort, around 2/3 of cases of MI were clinically silent
PATHOS (Agnelli et al., 2006) [35]	Observational study	755 patients hospitalized for acute stroke or TIA (aetiology unspecified)	PAD is common and associated with worse outcomes in patients with stroke or TIA ABI ≤ 0.9 was found in 33.5% of patients ABI ≤ 0.9 was associated with a 1.5-fold increased risk of adverse 1-year outcomes
Busch et al., 2009 [7]	Observational study	204 patients with acute ischaemic stroke or TIA followed for a mean of 2.3 years; included 46 cases with a confirmed atherosclerotic aetiology	PAD is associated with worse outcomes in patients with stroke or TIA In the overall cohort, ABI ≤ 0.9 at baseline was associated with a significantly higher rate of stroke, MI or death (12.8 vs. 6.4%; $p = 0.03$)
SCALA (Weimar et al., 2007; Weimar et al., 2008) [20, 36]	Observational study	852 patients hospitalized for ischaemic stroke or TIA from 85 stroke units across Germany. Did not exclude non-atherosclerotic aetiology	Asymptomatic PAD is much more common than symptomatic PAD 51% of patients had an ABI ≤ 0.9 Only 10% had classic PAD symptoms, such as intermittent claudication or signs of critical limb ischaemia PAD (symptomatic and asymptomatic) is associated with worse outcomes in patients with stroke or TIA After 17.5 months, a 2-fold higher risk of recurrent stroke or cardiovascular death was reported in patients that had experienced a stroke or TIA with an ABI ≤ 0.9 compared with patients with an ABI > 0.9
GetABI (Diehm et al., 2009) [8]	Epidemiological study	6,880 unselected patients (≥ 65 years) from primary care	Asymptomatic PAD is common in an unselected primary care population ABI ≤ 0.9 was found in 30.3% of patients with cerebrovascular disease ($n = 607$) Asymptomatic PAD has a similar comorbidity and risk-factor profile to symptomatic PAD 5-year all-cause mortality risk was not significantly different between asymptomatic and symptomatic PAD patients

¹ Asymptomatic carotid artery stenosis, diagnosed by colour-coded duplex sonography or digital subtraction angiography demonstrating $\geq 70\%$ stenosis. ² Measured using the European Carotid Surgery Trial method.

The difficulties associated with the post-discharge care of high-risk polyVD patients are not adequately addressed in the current guidelines. Specifically, the guidelines do not address practical issues such as the lack of information for patients regarding the benefits and services available, as well as detailed explanations about their condition [25]. In a 2-year follow-up study of patients admitted to hospital in New Zealand following an acute stroke, patients still had questions about their condition at both 6 and 24 months after admission [26]. Importantly, the type of information that they required changed over this 2-year time period, with questions on the basic aspects of stroke decreasing over 2 years and questions on the psychological impact of stroke increasing. Providing patients with booklets only is not sufficient to improve patient satisfaction and will not necessarily improve the care perceived by patients [27].

Following discharge from hospital, patients are recommended to adhere to guideline therapy for the secondary prevention of cardiovascular events. However, patient adherence is often not optimal. For example, a study of anti-hypertensive drugs used to control cardiovascular risk factors in elderly patients with grade I or II hypertension found that only 34% of patients fully adhered to their prescribed diuretics after 24 months [28]. In fact, adherence to any cardiovascular drug following an acute MI, has recently been shown to be low in patients discharged from hospital with as few as 44% of patients adhering to their recommended treatment with clopidogrel [29]. Despite these results, patients' adherence to therapies can be improved by relatively simple interventions, as shown in studies of patients with atherothrombotic disease [30, 31]. A visit to the cardiologist or primary care physician by the patient less than 1 month after discharge after acute MI, for example, is associated with higher rates of evidence-based medication use [30]. Furthermore, improved communication between the physician and patient was shown to increase patient compliance with β -blocker after acute MI [31].

The OSCARE Initiative

Currently, there is no standardised care protocol addressing the optimised treatment and management of patients with stroke and polyVD. There is need for protocols focussing on:

- Screening for polyVD
- Optimised treatment and discharge for stroke patients with polyVD
- Transfer of care for long-term follow-up

OSCARE is an initiative that has been set up to address some of the challenges associated with the care of all high-risk patients receiving inpatient hospital treatment for acute and recent ischaemic stroke, with particular focus on the management and treatment of high-risk stroke patients with polyVD. The aims of OSCARE are to continue the optimal treatment following discharge, to increase the adherence of the patients and to optimise risk factor control.

The OSCARE initiative will be evaluated in a single-centre pilot study with consecutive non-cardioembolic stroke patients with polyVD receiving the OSCARE approach (n = 100) or a usual-care approach (n = 100). Follow-up will be 1 year. One important aim of OSCARE is to identify the highest risk patients for a new vascular event. Patients will be screened for standard risk factors (such as arterial hypertension, diabetes, lipids, and smoking habit, among others), cardiovascular disease (ECG, patient history), peripheral arterial disease (ABI measurement) and carotid disease (through determination of intima-media thickness). Patients will be included in the study if they had a symptomatic or asymptomatic vascular disease in at least one other vascular bed (coronary or peripheral). Patients from the OSCARE group will receive a standardised transfer of care document including patient information that summarises the findings of the screening for polyVD, highlights the increased risk of these patients and underscores the importance of an optimised treatment. In addition, these patients will receive regular reviews every 3 months by a specifically trained vascular nurse. During the review, the following points will be addressed:

- Adherence to medication
- Risk factor control (revised personal risk factor documents)
- Quality of life
- Blood pressure (3 measurements over a 30-min period)
- What can be done to improve adherence to treatment?
- Regular follow-up appointments
- Patient education

After the follow-up, the OSCARE approach was compared to the usual-care approach with regard to medication adherence, risk factor control (blood pressure, diabetes, hyperlipidemia, smoking; primary endpoints) and occurrence of new vascular events defined as a composite of MI, stroke and vascular death (secondary endpoint). It is hypothesised that the OSCARE group shows a significantly ($p < 0.05$) improved medication adherence and risk factor control as well as a lower rate of new vascular events.

Table 2. Discharge documentation for stroke patients with polyVD

Document	Information included
Letter to primary care physician	Description of discharge materials Standard form from the specialist containing information such as diagnosis, lifestyle advice, follow-up appointments specific for the patient
Transfer of care	History of vascular events Medication history List of diagnostic tests carried out during hospital stay Blood pressure measurements Lipid measurements Liver function test measurements ECG report Smoking history Alcohol intake Identification of other risk factors for stroke Results of ECG, carotid Doppler, brain MRI and CT scan (including details of final diagnosis and stroke type) Results of screening for polyVD (including cardiovascular investigations, ABI measurements) Recommendation for carotid endarterectomy where appropriate Secondary prevention strategy (including rationale for managing high-risk patients) Details of discharge medication (including intended duration of therapy) Details of changes to medication and rationale for these changes Recommendation for long-term follow-up
Transfer of care medication document	Medications prescribed to the patient within hospital care Contain space for primary care physicians to detail when and why medications are altered post-discharge
Patient information pack, tailored to the individual needs of the patient	What you should know about PAD Stroke and PAD (patient information booklet) Stroke warning card Stroke and PAD passport Patient progress diary 'Looking after yourself after you have had a stroke' patient leaflet providing medication details and importance of medication adherence
Physician information pack	Slide kit and booklet describing slides
Other information	ABI measurement calculator Assessment of risk for further ischaemic events and PAD Follow-up questionnaire

Development of Materials

As part of the initiative to improve the care available for patients who have experienced a stroke, OSCARE is developing a range of web-based materials to assist in the transfer of patients from hospital to community care. These materials will also help to support the long-term care of patients in the community. Transfer should ensure the smooth continuation of optimal therapy, to increase both the quality of life and satisfaction of patients. Discharge of patients from hospitals must, therefore, be completed in a way that is well planned to ensure maximum satisfaction from both patients and carers, and in a

way that encourages communication between healthcare professionals, carers and patients [32, 33].

Materials under development by OSCARE to aid the switch from hospital to community care include transfer of care documentation, patient information and support documents (table 2). The transfer of care documentation prepared before discharge from hospital for each patient could help to ensure that the transfer of patient care from hospital to community care occurs in an optimal and effective manner.

The discharge materials being developed by OSCARE aim to help in the delivery of continued optimal care for

high-risk stroke patients by keeping all relevant stakeholders fully informed of the medical history and treatment of each patient, and ensuring that all details provided are comprehensive and up to date. Consequently, it is hoped that this initiative will improve physician and patient adherence to optimal therapy and that it will help support an integrated multidisciplinary approach to care in the community.

Conclusions

Stroke patients with polyVD are at an increased risk of secondary cardiovascular events, which can lead to high hospital readmission rates. Although there is evidence that suggests there is a high prevalence of polyVD in patients who have experienced a stroke, polyVD is often not detected, potentially resulting in suboptimal management of the disease. Despite the clinical need to manage high-risk stroke patients more effectively, current evi-

dence-based guidelines do not adequately address the detection and treatment of polyVD in stroke patients. These issues must therefore be addressed to provide patients with the best possible treatment. OSCARE is an initiative set up to reduce these shortcomings, and aims to increase the awareness and promote the investigation of potential polyVD in stroke patients. By highlighting the full extent of the risks associated with this high-risk population, OSCARE aims to provide the optimum care for stroke patients with polyVD.

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